IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

Paul Douglas CLARKE

Attn: Applications

Serial No.: National Stage Application based on
International Application PCT/GB00/02825

Filed: January 17, 2002

For: ANTISEPTIC COMPOSITION

CONFIRMATION CLAIM FOR PRIORITY

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

The benefit of the filing date of the following foreign application filed in the following foreign country and priority provided in the 35 USC §119 have been claimed for the above-identified application:

Great Britain Application No. 9917040.9, filed July 21, 1999.

A copy of the priority document was filed in the International Stage (PCT).

It is requested that the file of this application be marked to indicate that the requirements of 35 USC §119 have been fulfilled and that the Patent and Trademark Office kindly acknowledge receipt of these papers.

Respectfully submitted,

TPP:mat
Attorney Docket No.: TPP 31435

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Registration No. 31,689

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Date: January 17, 2002

THE APPLICANT HEREWITH PETITIONS THE PTO TO EXTEND THE TIME FOR RESPONSE AS REQUIRED TO MAKE THE ATTACHED DOCUMENT TIMELY FILED. PLEASE CHARGE THE COST THEREOF TO DEPOSIT ACCOUNT 19-4375

STEVEN DAVIS MILLER & MOSHER, L.L.P.

PCT/GB00/02825

10/031170

The Patent Office
Concept House
Cardiff Road
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PRIORITY DOCUMENT

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GB00/02825

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I, the undersigned, being an officer duly authorised in accordance with ~~Section 74(1) and (4)~~ of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

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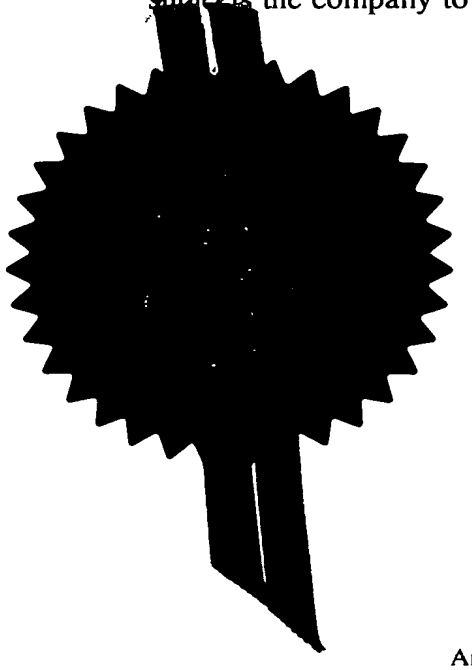

Signed Andrew Gerry

Dated 28 July 2000

Form 1/77

Patents Act 1977
(Rule 16)

The Patent Office

THE PATENT OFFICE
A
21 JUL 1999
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Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office

Cardiff Road
Newport
Gwent NP9 1RH

1. Your reference — CPW/ADN

2. Patent application number *(The Patent Office will fill in this part)* — **9917040.9** — 21 JUL 1999

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

PAUL DOUGLAS CLARKE,
51 Gower Street,
London WC1E 6HJ

Patents ADP number *(if you know it)* 73193790002

If the applicant is a corporate body, give the country/state of its incorporation

4. Title of the invention — ANTISEPTIC COMPOSITION

5. Name of your agent *(if you have one)*

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

A.A. THORNTON & CO.
NORTHUMBERLAND HOUSE,
303-306 HIGH HOLBORN,
LONDON. WC1V 7LE

Patents ADP number *(if you know it)* 75001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*
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7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*
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8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*

a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
See note (d))

NO

[redacted]nts Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	
Description	6
Claim(s)	–
Abstract	–
Drawing(s)	–

10. If you are also filing any of the following, state how many against each item.

Priority documents	–
Translations of priority documents	–
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	–
Request for preliminary examination and search *(Patents Form 9/77)*	–
Request for substantive examination *(Patents Form 10/77)*	–
Any other documents *(please specify)*	–

11. I/We request the grant of a patent on the basis of this application.

Signature A A Thornton & Co. Date 21/07/99

12. Name and daytime telephone number of person to contact in the United Kingdom MR. C. P. WAIN 01604 638242

Warning

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

ANTISEPTIC COMPOSITION

The present invention relates to an antiseptic composition.

It is known that a number of natural products have insect repellent properties. Citriadora oil obtained from various species of eucalyptus is one example of such a natural product, citronella oil which is obtained from certain grasses is another. We have previously investigated certain insect repellent natural products and have found that the insect repellent properties are in a fraction rich in p-menthane-3,8-diol (PMD). This is described in our GB-A-2282534.

We have now found, very surprisingly, that PMD not only has insect repellent properties but also possesses the totally unrelated quality of antiseptic properties. Thus, we have observed antiseptic activity of the compound against certain microbes and, in particular and most importantly, against two strains of multiply resistant *Staphylococcus aureus* (MRSA). It appears, therefore, that PMD will have general antiseptic utility and be particularly useful, at least in respect of certain microbes, as a bactericide as well as being fungicidal and capable of acting as an antibiotic.

According to one aspect of the invention, we provide the use of PMD as an antiseptic. According to a further aspect of the invention, there is

provided the use of PMD as an antibiotic. According to a further aspect, the invention provides the use of PMD as a fungicide and/or bactericide

The PMD for use in the present invention may be derived from a natural source or may be synthetic, or a mixture of the two. A preferred source of natural PMD is the lemon eucalyptus plant. Synthetic PMD may be obtained by any route, for example, such as described by Zimmerman and English in J.A.C.S. 75 (1953) pp 2367-2370.

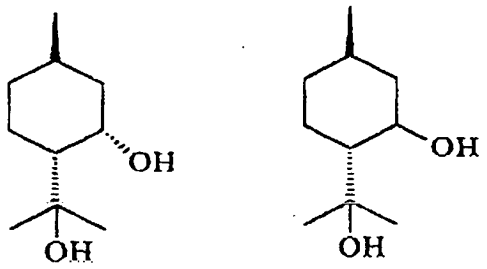
The PMD for use in the present invention may be a substantially pure form of the compound, or a crude extract, for example from a natural source. An example of a crude extract is a PMD-rich extract derived from lemon eucalyptus. The PMD can be produced by cyclisation of citronellal which is present in high concentration in lemon eucalyptus oil (approximately 75% by weight). We have obtained a PMD-rich extract from the lemon eucalyptus oil which includes both geometric isomers of PMD usually at about 64% by weight. The crude extract also includes citronellol and isopulegols plus certain other minor components.

According to a further aspect of the invention, there is provided the use of a PMD-rich extract containing composition, which extract is derived from natural lemon eucalyptus oil, as an antiseptic. We market this crude extract under the trade mark "Citriodiol".

It is known that eucalyptus oils include certain components, such as cineoles, which are known to have antiseptic properties. For the avoidance of doubt, we make no claim to the antiseptic activity of any component, other than PMD when it is derived from a natural source.

A composition for use in accordance with the invention can comprise PMD and a carrier. PMD is poorly soluble in water, so that it is preferred to use an oil as a carrier, or use a solvent, such as alcohol, for water-based compositions.

It is known that PMD exists in two geometric isomeric forms, namely the cis and trans isomers, and that there are two enantiomers for each geometric isomer.



trans cis

Our experimental work is based on a substantially pure racemic optical mixture of the cis isomer. It is, however, understood that the claimed activities for PMD are common to all its isomeric forms.

In a further aspect of the invention, the composition for use in the invention comprises only one of the isomers of PMD, with a carrier therefor.

It is a further aspect of the invention that the relative amounts of cis:trans PMD isomers in the compositions for use in the present invention are varied as desired. This can be done by mixing previously separated isomers in the appropriate ratio, or by adjusting the ratio in a mixture of naturally occurring or synthetic source.

In tests we have found that PMD is effective against certain strains of MRSA. In a further aspect, therefore, the invention provides the use of PMD against MRSA.

The uses of the present invention may be adopted in sanitizing a surface, for example in a hospital room or ward. For these uses, the composition including PMD is desirably formulated for spray application. In a particularly preferred mode of application, the spray is an electrostatic spray. In this, charged particles of the composition including PMD are projected as a fine mist. Becaus all the particles carry a similar, for example positive, charge

they repel each other, but are attracted to an oppositely charged surface. By this means of spraying, a very good coverage of the composition on the surface may be obtained. Devices for electrostatically spraying the composition for use in the invention will be known to the person skilled in the art.

A spray may also be used, for example, for dispensing a composition including PMD onto a hand (or other part) of a person. The actuation of the dispenser may be by means of an infra-red sensor, for example, so that the person need not contact a surface, and thereby risk the transfer of microbes to or from their hand. Electrostatic spray application to a hand may be used, with advantage, where a substantially uniform coverage of antiseptic is particularly important e.g. to a surgeon during "scrubbing up" before surgery. To increase the likelihood of the charged particles covering the skin surface, desirably the electrostatic spray nozzles may be arranged to spray into the interior of a cabinet or container as the hand is introduced therein.

PMD may also be included as a component in household detergents, cleansers and creams, for example, washing powders or conditioners and hand gels.

Furthermore, PMD may be impregnated into household objects which may be prone to microbial infestation and so risk infecting inhabitants, e.g. dishcloths, plastic soap dishes, surfaces used for the preparation of food.

A composition including PMD can also be used in medicine. For example, it can be applied to broken skin, or it may be an ingredient in throat lozenges or pastilles. In this aspect, the invention provides PMD for use as an antiseptic, antibiotic or fungicide.

PMD is the active ingredient in our "Mosiguard" ™ insect repellant. We have conducted tests to show regulatory authorities that PMD is not toxic, and we have marketed our insect repellent for several years and there has been no report of any significant toxicity thereof. Potentially, therefore, the medical uses of PMD may be topical or systemic. Systemic administration

may be by way of an oral dosage form or by a parenteral route, such as by intro-venous injection.

In a further aspect, the invention provides the use of PMD in the manufacture of an antiseptic, antibiotic or fungicidal medicament.

In medical uses the PMD may be formulated with the carrier as a cream, or, as mentioned above, as a throat lozenge or pastille. One cause of dandruff is known to be of fungal origin. PMD may be included as an ingredient in an anti-dandruff shampoo in order to combat the scalp infection.

A further specific medical use is based upon the fact that many carriers of staphylococcus bacteria carry the bacterium in their nasal passages. A composition including PMD may be applied to the accessible inner surfaces of the nose in order to control or eliminate bacteria which may cause regular systemic effects.

Another specific medical use is in wound irrigation during surgery e.g. surgery conducted in the peritoneal cavity.

A PMD-rich extract may be obtained from PMD-containing material, such as the leaves of a eucalyptus plant. A preferred source of PMD-rich extract is obtained by stirring eucalyptus citriadora oil derived from the plant with dilute sulphuric acid (usually 5% sulphuric acid), as previously explained in our GB-A-2282534.

In order that the invention may be fully understood, the following Example is given by way of illustration only.

Example

Cis PMD MIC/MBC Determination

MIC - minimum inhibitory concentration. This is the concentration of PMD which prevents bacterial growth. A "+" indicates bacterial growth, whereas a "-" indicates that bacterial growth is prevented. Thus, for E. Coli below, the minimum inhibitory concentration is 0.25% PMD in 1.25% ethanol.

MBC - minimum bactericidal concentration. This is the concentration of PMD which kills the bacteria. A "✚" indicates live bacteria are present. Therefore, for E. Coli, the minimum bactericidal concentration is 0.5% PMD in 2.5% ethanol i.e. the concentration immediately above that which does not kill the bacteria.

Cis PMD was dissolved in Absolute Ethanol (0.2 g/ml) to give 20% solution. This was further diluted in water to give 10% in 50% EtOH. 200 µl was added to 0.8 ml Iso-sensitest broth to give a 2% solution in 10% EtOH. Serial 2-fold dilutions in ISB were then carried out and 20 µl E.coli (McFarlane 0.5) were added to each tube and incubated overnight at 37°C. After 18 hours, tubes showing no growth were sub-cultured.

	Percentage Concentrations					
Sample	2	1	0.5	0.25	0.125	0.06
E.coli	-	-	-	- ✚	+ ✚	+ ✚
S.aureus (oxford)	-	-	- ✚	+ ✚	+ ✚	+ ✚
P.aeruginosa	-	-	- ✚	+ ✚	+ ✚	+ ✚
MRSA 15	-	-	- ✚	+ ✚	+ ✚	+ ✚
MRSA 16	-	-	- ✚	+ ✚	+ ✚	+ ✚
S.pyogenes	-	-	-	- ✚	+ ✚	+ ✚
Alcohol concentration	10%	5%	2.5%	1.25%	0.6%	0.3%
Control: Alcohol only /E.coli		✚	✚	✚	✚	✚